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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT: XRM-5313 (formulation containing DE-498 and Trifluralin) - Experimental Use Permit

ToxChem No.: 889
HED Project No.: 1-2384

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Toxicology Branch II
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Registrant: DowElanco
9002 Purdue Road
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The registrant (DowElanco) has submitted 7 studies in support of an Experimental Use Permit for evaluation of preemergence control of annual grasses and broadleaf weeds in soybeans. These studies have been evaluated, and the Data Evaluation Reports are attached. The conclusions are as follows:

1. Acute Oral Toxicity in Rats (Guideline 81-1) - MRID No. 4419938-05

   The test material was administered to male and female Fischer 344 rats by a single oral gavage at dosages of 500, 2000, and 5000 mg/kg. No rats died at 2000 mg/kg and all died at 5000 mg/kg.

   LD_{50} (Males & Females) = Between 2000 and 5000 mg/kg
   Toxicity Category: III (from 500 through 5000 mg/kg)

   CORE Classification: Guideline

2. Acute Dermal Toxicity in Rabbits (Guideline 81-2) - MRID No. 419938-06

The test material was administered to male and female New Zealand White rabbits by a single 24-hour dermal application at a dosage of 2000 mg/kg. There were no mortalities or signs of systemic toxicity at this dose. Dermal observations included erythema, edema, fissuring, scaling, and crusting.

LD_{50} (Males & Females) = Greater than 2000 mg/kg
Toxicity Category: At least III (from 2,000 through 5,000 mg/kg)

CORE Classification: Guideline

3. Acute Inhalation Toxicity in Rats (Guideline 81-3) - MRID 420033-02

The test material was administered by 4-hour exposure to male and female Fischer 344 rats at an aerosol exposure level of 5.92 mg/L. There were no mortalities and no signs of systemic toxicity.

LC_{50} (Males & Females) = Greater than 5.92 mg/liter
Toxicity Category: IV (greater than 5 mg/liter)

CORE Classification: Guideline

4. Primary Eye Irritation in Rabbits (Guideline 81-4) - MRID 419938-07

Six New Zealand White rabbits (3/sex) were exposed to a single 0.1 ml dose of the test material in the conjunctival sac of the right eye and observed for 21 days. Reversible conjunctival redness, progressing to chemosis with discharge, was noted by 24 hours postdose. Some corneal opacities observed at 24 hours postdose were still present at Day 21.

Toxicity Category: I (corneal opacity was not reversible within 21 days)

CORE Classification: Guideline

5. Primary Dermal Irritation in Rabbits (Guideline 81-5) - MRID 419938-08

Six New Zealand White rabbits received a single 0.5 ml dermal dose of the test material, with exposure lasting 4 hours. The study was terminated at 14 days. Slight erythema and edema were noted at 72 hours and were reversed by 7 days. Slight to marked desquamation was observed on days 7 and 14.

Toxicity Category: IV (mild or slight irritation at 72 hours)

CORE Classification: Guideline

6. Dermal Sensitization in Guinea Pigs (Guideline 81-6) - MRID 419938-09

For the induction phase, the test material was administered as a 50% solution in dipropylene glycol monomethyl ether, once weekly for 3 weeks by dermal application to Hartley albino guinea pigs. A single 50% test substance solution served as the challenge dose, administered dermally approximately 2 weeks after the last induction dose; slight to moderate erythema was noted 24 and 48 hours postdose.

The test material was determined to be a sensitizing agent.

CORE Classification: Minimum

7. 21-Day Dermal Toxicity in Rabbits (Guideline 82-2) - MRID 419938-10

The test material was applied undiluted to the skin of New Zealand White rabbits (5/sex/group) at doses levels of 100, 500, and 1000 mg/kg/day. The rabbits were exposed for 6-hour periods on a total of 15 days of the 21-day study duration. Dose- and treatment-related dermal irritation was noted at all dose levels. There were no signs of systemic toxicity.

NOEL (dermal effects) = Not determined
LOEL (dermal effects) = 100 mg/kg/day

NOEL (systemic effects) = At least 1000 mg/kg/day
LOEL (systemic toxicity) = Not determined

CORE Classification: Guideline

Recommendation:

The registrant, DowElanco, requests that an Experimental Use Permit be issued and tolerances be established for XRM-5313 for the preemergence control of annual grasses and broadleaf weeds in soybeans. DowElanco requests that the temporary tolerances proposed for expected residues of DE-498 in or on soybeans (62719-EUP-RA; Petition #1G4006) be applied to XRM-5313 and states that this petition is supported by the existing tolerances for Trifluralin.

The Toxicology Branch (II) cannot currently address this petition for the following reasons:

1. The request for an Experimental Use Permit and proposed temporary tolerance for expected residues of DE-498 in or on soybeans (62719-EUP-RA; Petition #1G4006) was submitted to the Agency on June 17, 1991. The petition, along with the supporting data, is currently in review, but has not yet been completed.

2. The tolerance regulation for Trifluralin (40 CFR 180.207) does not contain an established tolerance for residues of Trifluralin in or on soybeans.

Upon resolution of these insufficiencies, the application for an EUP for XRM-5313 can be addressed and resolved.

U.S. ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PESTICIDES/HED/SACB
TOX ONELINERS

TOXCHEM NO. 889: XRM-5313

CITATION	MATERIAL	ACCESSION/ MRID. NO.	RESULTS	TOX CAT	CORE GRADE/ DOCUMENT #
81-1 Acute Oral Toxicity Species: rat Dow Chemical, Toxicology Research Laboratory; M-005313-002A; 05/31/91	XRM-5313; formulation containing 2.6% XRD-498 and 35.8% Trifluralin	419938-05	Dosed by single oral gavage to male and female Fischer 344 rats (5/sex) at doses of 500, 2000, and 5000 mg/kg. No rats died at 2000 mg/kg and all died at 5000 mg/kg. LD_{50}(Males and Females) = Between 2000 and 5000 mg/kg.	III	Guideline
81-2 Acute Dermal Toxicity Species: rabbit Dow Chemical, Toxicology Research Laboratory; M-005313-002D; 05/23/91	XRM-5313; formulation containing 2.6% XRD-498 and 35.8% Trifluralin	419938-06	Single 24-hour dermal application to male and female NZW rabbits at a dose of 2000 mg/kg. No mortalities or signs of systemic toxicity; dermal observations included erythema, edema, fissuring, scaling, and crusting. LD_{50}(Males and Females) = Greater than 2000 mg/kg.	III	Guideline
81-2 Acute Inhalation Toxicity Species: rat Dow Chemical, Toxicology Research Laboratory; M-005313-001; 05/22/91	XRM-5313; formulation containing 2.6% XRD-498 and 35.8% Trifluralin	420033-02	4-hour exposure to male and female Fischer 344 rats (5/sex) at an aerosol exposure level of 5.92 mg/L. No mortalities and no signs of systemic toxicity. LC_{50}(Males and Females) = Greater than 5.92 mg/liter.	IV	Guideline
81-4 Primary Eye Irritation Species: rabbit Dow Chemical, Toxicology Research Laboratory; M-005313-002C; 05/17/91	XRM-5313; formulation containing 2.6% XRD-498 and 35.8% Trifluralin	419938-07	Single 0.1 ml dose in the conjunctival sac of the right eye to six NZW rabbits (3/sex); observations for 21 days. Reversible conjunctival redness, progressing to chemosis with discharge, noted by 24 hours postdose. Some corneal opacities observed at 24 hours postdose still present at Day 21.	I	Guideline
81-5 Primary Dermal Irritation Species: rabbit Dow Chemical, Toxicology Research Laboratory; M-005313-002B; 05/15/91	XRM-5313; formulation containing 2.6% XRD-498 and 35.8% Trifluralin	419938-08	Single 0.5 ml 4-hour dermal dose of the test material to six NZW rabbits; [illegible]. Slight erythema and edema noted at 72 hours and reversed by 7 days. Slight to marked desquamation observed on days 7 and 14.	IV	Guideline
81-6 Dermal Sensitization Species: guinea pig Dow Chemical, Toxicology Research Laboratory; M-005313-002E; 05/31/91	XRM-5313; formulation containing 2.6% XRD-498 and 35.8% Trifluralin	419938-09	Induction phase: 50% solution in dipropylene glycol monomethyl ether applied dermally once weekly for 3 weeks to Hartley albino guinea pigs. Challenge: single dermal application of 50% solution, approximately 2 weeks after the last induction dose. Slight to moderate erythema noted 24 and 48 hours postdose. Judged to be a skin sensitizing agent.		Minimum
82-2 21-Day Dermal Species: rabbit Dow Chemical, Toxicology Research Laboratory; M-005313-003; 05/17/91	XRM-5313; formulation containing 2.6% XRD-498 and 35.8% Trifluralin	419938-10	6-hour dermal applications to the skin of NZW rabbits (5/sex/group) at doses levels of 100, 500, and 1000 mg/kg/day for a total of 15 days of the 21-day study duration. Dose- and treatment-related dermal irritation noted at all dose levels; no signs of systemic toxicity. Dermal effects: NOEL = not determined; LOEL = 100 mg/kg/day. Systemic toxicity: NOEL = At least 1000 mg/kg/day; LOEL = Not determined.		Guideline

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